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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,498	XIANG ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-11 and 63-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 6-11, 63-70* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 7, 2003 has been entered.

The Amendment filed August 18, 2003 in response to the Office Action of October 14, 2003 is acknowledged and has been entered as requested in the RCE filing November 7, 2003. Claims 2, 3 and 12-62 have been cancelled. Claims 63-70 have been added. Claims 1, 4-11 and 63-70 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Drawings

The office acknowledges the corrections to the drawings submitted August 21, 2003. The drawing have been approved by the Draftsperson.

Claim Objections

The objection of claim 5 because of the following informalities **is maintained**: The claim is objected to because it is dependent on a rejected claim. SEQ ID NO: 1 is free of the prior art of record. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1, 4, 6-11 and newly added claims 63-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is maintained** for reasons of record.

The specification only indicates that the sequence be **capable of yielding** an infectious GBV-C particle from an infected cell (see specification page 19, lines 1-2). Neither the specification nor the declaration by Jack Stapleton M.D. (submitted February 28, 2003 and August 21, 2003) have defined the structures which distinguishes the instantly claimed the nucleic acid molecule as "infectious" over the prior art molecules. The declaration by Jack Stapleton M.D. (submitted August 21, 2003) which asserts that a nucleic acid construct that is very similar to the instant SEQ ID NO: 1 (see Kim et al. U.S. Pat. No. 5874563, SEQ ID NO: 14) does not yield particles which are infectious. Yet a review of the two sequences indicates that the sequence differences are located throughout the entire 9395 nt sequences, therefore, the feature that makes the instant molecule infectious cannot be correlated with a specific structure. It remains unclear how Applicant's nucleic acid sequence yields and infectious clone while the prior art references using a similar experimental procedure set out in the instant specification does not. The claims remain unclear by what is intended by "infectious".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claim 1-4, 6-11 and newly added claims 63-70 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an infectious full-length clone of GBV-C set out in SEQ ID NO:1, does not reasonably provide enablement for an infectious nucleic acid that is less-than or greater-than the full-length clone is maintained for reasons of record.

Applicants' arguments have been fully considered but are not deemed persuasive. Applicants' arguments are that the Pang et al. reference cited by the Office is directed to a dengue virus and not a hepatitis virus, and that the Pang et al. reference had a goal that was very different from the instantly claimed invention. In response to applicant's argument that *Pang et al.* reference is nonanalogous art, because it does not specifically address problems with GBV-C and thereby would not be relevant for an enablement rejection. It has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, *Pang et al.* utilize a flavivirus construct (the instantly claimed GBV-C is also a flavivirus) although the authors goal may not have been to construct an infectious molecule the reference does not have to have the same goal as the claimed invention. The reference clearly shows that a virus construct from the same family of viruses, will allow for the replication of the heterologous nucleic acid but they do not produce

particles and are thereby not infectious. The reference clearly indicates that more is required in order to produce an infectious nucleic acid. Neither the art nor the instant specification have provided any guidance as to the structural requirements of the nucleic acid that is necessary to produce an "infectious" particle.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. Such an analysis does not need to specifically enumerate (points 1-8) but only needs to have a select few of the factors present discussed in a rejection.

The specification shows a single example of an "infectious" DNA set out in SEQ ID NO:1. The instant fact pattern fails to disclose any particular structure for the claimed "infectious" DNA that encodes an amino acid sequence that is 70% identical to SEQ ID NO:2. The specification does not provide any guidance or any working examples in this unpredictable art, and thus the artisan would have been unable to have prepared the claimed "infectious" DNA without undue experimentation. Furthermore an assay for finding a product (measuring particle release from a transfected cell) is not equivalent to a positive recitation of how to make such a

product. This claim fails to meet the enablement requirement for the "how to make" prong of 35 U.S.C. § 112 first paragraph.

Applicants declaration indicates that a nucleic acid that shares 91% similarity with the instantly claimed sequence of SEQ ID NO:1 (see Kim et al. U.S. Pat. No. 5874563; SEQ ID NOs: 14 and 182) does not produce virus particles from a transfected cell. A comparison of a prior art nucleic acid (Kim et al. U.S. Pat. No. 5874563) which is 91% identical to the nucleic acid of SEQ ID NO: 1 of the instant invention (see declaration by Jack Stapleton M.D. submitted August 21, 2003) indicates that prior art DNA is not able to produce virus particles in a transfected cell. It is important to note that the differences between the prior art nucleic acid and the nucleic acid of the instant invention are found spread throughout the sequence and cannot be attributed to a single region which would imply that a specific identifiable structure is responsible for the "infectious character" of the nucleic acid of SEQ ID NO:1 of the instant invention. The specification provides only a single working example, they have shown that the cell culture supernatant from a full-length infectious GBV-C clone (SEQ ID NO:1) contains infectious virus. This was determined by incubating the supernatant with new uninfected cells (see example 4) and observing signs of infection. The description of a single example which utilizes the full-length clone does not provide sufficient guidance to make infectious clones that may be smaller or larger in size. The specification has not provided any information regarding the structural requirements necessary to make to make a GBV-C nucleotide sequence "infectious". Therefore, without specific guidance or direction and /or working examples, one of ordinary skill in the art would not be able to reproducibly practice the entire scope of the invention as claimed, without undue experimentation.

Claims 1, 4, 6-11 and 63-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was ready for patenting" such as by the use of drawings or structural chemical formulas that show that the invention was complete, or describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

> (MPEP 2163) The satisfaction of the enablement requirement does not satisfy the written description requirement. See *In re Barker*, 559 F.2d 588, 591, 194 USPQ 470, 472 (CCPA 1977) (a specification may be sufficient to enable one skilled in the art to make and use the invention, but still fail to comply with the written description requirement). See also *In re DiLeone*, 436 F.2d 1404, 1405, 168 USPQ 592, 593 (CCPA 1971). For the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998).

In this instance applicants are claiming an "infectious" GBV-C DNA encoding an amino acid sequence that is at least 70% identical to SEQ ID NO:2, or an infectious clone comprising 500, 1000, 2000 or 5000 nucleotides of SEQ ID NO: 1. The structure necessary to provide the "infectious" character to nucleic acid sequences that are 500, 1000, 2000 or 5000 in length have not been sufficiently described in terms of their structure and function. Applicants are claiming and "infectious" DNA, where the product is defined based on function alone without providing any information regarding the structure. Claiming a product based on function does not provide sufficient description of the product. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Applicants' declaration by Jack Stapleton M.D. (submitted August 21, 2003) indicates that similar full-length structures do not behave the same using similar experimental procedures. Therefore, structurally unrelated "molecules" encompassed by the claimed invention other than those disclosed in the specification as filed would be expected to have greater differences in their functional characteristics and attributes. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required.

"a mere wish or plan" for obtaining an invention is not enough to comply with § 112, ¶ 1(*Regents of the University of California v. Eli Lilly & Co., 119* F.3d 559, at 1566).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was

in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

The instant specification and claims do not provide sufficient functional and structural characteristics of the DNA that provides the "infectious" character to the GBV-C DNA. Since the disclosure fails to describe the common attributes or characteristics that identify members of the group, the disclosure of single compound is insufficient to describe the genus of molecules, encompassed by the claimed invention. Therefore, there is lack of written description in the instant invention for GBV-C infectious clones that have a structure other than the structure disclosed in SEQ ID NO:1

Claimed invention is drawn to an isolated and purified DNA encoding GBV-C identified by the function of being "infectious' which is measured by the method of determining whether virus particles can be recovered from a transfected cell. However, no structural characteristics of the DNA have been elucidated at the time of filing of the instant invention. A comparison of a prior art reference nucleic acid (Kim et al. U.S. Pat. No. 5874563) which is 91% identical at the nucleic acid level to SEQ ID NO: 1 of the instant invention (see declaration by Jack Stapleton M.D. submitted August 21, 2003) indicates that prior art DNA is not able to produce virus particles in a transfected cell. It is important to note that the differences between the prior art nucleic acid and the nucleic acid of the instant invention are found spread throughout the sequence and cannot be attributed to a single region which would imply that a specific identifiable structure is responsible for the "infectious character" of the nucleic acid of SEQ ID NO:1 of the instant invention. There no indication that the artisan actually implemented the method of measuring particle release to determine if a structured is "infectious" so as to identify

any other structures or structures that are less than the full length structure of SEQ ID NO:1. This situation is analogous to that of *Regents of the University of California v Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Because one skilled in the art would conclude that the inventors were not in possession of the claimed invention. The claims fail to comply with the written description requirement.

Claim Rejections - 35 USC § 102

The rejection of claims 1-4, 6, 7 and 9-10 under 35 U.S.C. 102(b) as being anticipated by Kim et al. (U.S. Pat. No. 5,856,134, see IDS) **is withdrawn** for in view of the submission of Applicants' declaration of August 21, 2003. The declaration does not specifically state that the same experimental procedures as those set out in the specification were used the experiments described in the declaration. The declaration is taken at face value to indicate the Kim et al. nucleic acid does not yield GBV-C particles while nucleic acid of the instant invention does produce such particles.

The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Xiang et al. (Journal of Virology, 1998, see IDS) **is withdrawn** for in view of Applicants' amendments to the claims.

The rejection of claims 1-3, 6 and 9-11 under 35 U.S.C. 102(e) as being anticipated by Pilot-Matias et al. (U.S.Pat. No. 6,156,495) **is withdrawn** for in view of Applicants' amendments to the claims.

Conclusion

Claims 1, 4, 6-11 and 63-70 are rejected.

Claim 5 is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

The official fax phone number for the organization where this application or proceeding is assigned is 703-872-9306; for informal communications please the fax phone number will change to 571-273-0912

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 2/9/04